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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER
LANDSMAN, ROBERT S

ART UNIT	PAPER NUMBER
1647	18

DATE MAILED: 08/01/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application N .	Applicant(s)	
	09/899,495	BENJAMIN ET AL.	
	Examin r	Art Unit	
	Robert Landsman	1647	

-- The MAILING DATE of this communication appears on the c ver sheet with the corresp ndence address --

Peri d f r Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 May 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disp sition of Claims

4)☒ Claim(s) *1-148* is/are pending in the application.

4a) Of the above claim(s) *1-104 and 110-148* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *105-109* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Pri rity under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *4,6* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *Sequence Comparisons A and B* .

DETAILED ACTION

1. Formal Matters

A. Claims 1-148 are pending in the application and were subject to restriction in Paper No. 7, dated 4/23/03. In Paper No. 8, filed 5/22/03, Applicants elected Group III, claims 30-35 and 104-109 as drawn to SEQ ID NO:116. In reviewing the claims, only claims 105-109 read on SEQ ID NO:116. Therefore, claims 105-109 are the subject of this Office Action. Applicants have argued that it would not be an undue burden to search the method claims of Group V along with Group III. If the product claims of Group III (claims 105-109) are found allowable, then method claims commensurate in scope with the product claims will be rejoined with the product claims as long as they do not raise any new issues under 35 USC 112. Elected claims depend from claims 104 and 75. These claims, though not considered elected claims, will be examined in case only since they have dependent claims which are elected and being examined. Applicants intend to include any of the limitations of these claims into any subsequently amended claim.

2. Title

A. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed. The following title is suggested: Human Ion Channel Proteins.

3. Claim Objections

A. Claims 105-109 are objected to since they recite either non-elected SEQ ID NOs (e.g. 115, 117, 118, 119), or depend from non-elected claims.

4. Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

A. Claims 105-109 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by a specific, substantial and credible asserted utility or a well established utility. These claims are directed to a polypeptide of SEQ ID NO:116. However, the invention encompassed by these claims has no apparent or disclosed patentable utility. This rejection is consistent with the current utility guidelines,

published 1/5/01, 66 FR 1092. The instant application has provided a description of an isolated protein. However, the instant application does not disclose a specific and substantial biological role of this protein or its significance.

However, it is clear from the instant specification that the claimed receptor is what is termed an "orphan receptor" in the art. The instant application does not disclose the biological role of the claimed protein or its significance. Applicants disclose in the specification that the claimed receptor is believed to be an ion channel protein. However, the basis that the receptor of the present invention is an ion channel protein is not predictive of a use. There is little doubt that, after complete characterization, this protein will probably be found to have a patentable utility. This further characterization, however, is part of the act of invention and, until it has been undertaken, Applicants' claimed invention is incomplete.

The instant situation is directly analogous to that of which was addressed in Brenner v. Manson, 148 U.S.P.Q. 689 (Sus. Ct, 1966), in which a novel compound which was structurally analogous to other compounds which were known to possess anticancer activity was alleged to be potentially useful as an antitumor agent in the absence of evidence supporting this utility. The court expressed the opinion that all chemical compounds are "useful" to the chemical arts when this term is given its broadest interpretation. However, the court held that this broad interpretation was not the intended definition of "useful" as it appears in 35 U.S.C. 101, which required that an invention must have either an immediate obvious or fully disclosed "real-world" utility. The court held that:

> "The basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility," "[u]nless and until a process is refined and developed to this point - where specific benefit exists in currently available form – there is insufficient justification for permitting an applicant to engross what may prove to be a broad field," and "a patent is not a hunting license," "[i]t is not a reward for the search, but compensation for its successful conclusion."

The specification discloses that the polynucleotides of the invention encode proteins which are believed to be ion channel proteins. However, the assertion that the disclosed protein of SEQ ID NO:116 has biological activities similar to known ion channel proteins cannot be accepted in the absence of supporting evidence, because generally, the art acknowledges that function cannot be predicted based solely on structural similarity to a protein found in the sequence databases. For example, Skolnick et al. (2000, Trends in Biotech. 18:34-39) state that knowing the protein structure by itself is insufficient to annotate a number of functional classes, and is also insufficient for annotating the specific details of protein function (see Box 2, p. 36). Similarly, Bork (2000, Genome Research 10:398-400) states that the error rate of functional annotations in the sequence database is considerable, making it even more difficult to infer correct function from a structural comparison of a new sequence with a sequence database (see

especially p. 399). Such concerns are also echoed by Doerks et al. (1998, Trends in Genetics 14:248-250) who state that (1) functional information is only partially annotated in the database, ignoring multi functionality, resulting in underpredictions of functionality of a new protein and (2) overpredictions of functionality occur because structural similarity often does not necessarily coincide with functional similarity. Smith et al. (1997, Nature Biotechnology 15:1222-1223) remark that there are numerous cases in which proteins having very different functions share structural similarity due to evolution from a common ancestral gene.

Brenner (1999, Trends in Genetics 15:132-133) argues that accurate inference of function from homology must be a difficult problem since, assuming there are only about 1000 major gene superfamilies in nature, then most homologs must have different molecular and cellular functions. Finally, Bork et al. (1996, Trends in Genetics 12:425-427) add that the software robots that assign functions to new proteins often assign a function to a whole new protein based on structural similarity of a small domain of the new protein to a small domain of a known protein. Such questionable interpretations are written into the sequence database and are then considered facts.

Therefore, based on the discussions above concerning the specific examples of structurally similar proteins that have different functions, along with the art's recognition that one cannot rely upon structural similarity alone to determine functionality, the specification fails to teach the skilled artisan the utility of the claimed polypeptide of SEQ ID NO:116 which appears to be homologous to other ion channel proteins. Therefore, the instant claims are drawn to a polynucleotide encoding a protein which has a yet undetermined function or biological significance. There is no actual and specific significance which can be attributed to said protein identified in the specification. Applicants do disclose a laundry list of diseases in the specification which may be affected by the protein of the invention; however, this is not a specific utility. For this reason, the instant invention is incomplete. In the absence of a knowledge of the natural ligands or biological significance of this protein, there is no immediately obvious patentable use for it. To employ a protein of the instant invention in the identification of substances which bind to and/or mediate activity of the said receptor is clearly to use it as the object of further research which has been determined by the courts to be a non-patentable utility. Since the instant specification does not disclose a "real-world" use for said protein then the claimed invention is incomplete and, therefore, does not meet the requirements of 35 U.S.C. 101 as being useful.

5. Claim Rejections - 35 USC § 112, first paragraph - enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

A. Claims 105-109 are rejected under 35 U.S.C. 112, first paragraph, as failing to adequately teach how to use the instant invention. Specifically, since the claimed invention is not supported by a specific, substantial and credible asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

B. Furthermore, if the present invention was found to have utility, claims 105-109 would still be rejected under 35 U.S.C. 112, first paragraph, because the specification, while then being enabling for SEQ ID NO:116, does not reasonably provide enablement for polypeptides which are "**homologous**" to any proteins, including those having "**at least one conservative amino acid substitution,**" or for nucleic acids encoding "**at least a portion**" of ion-x. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

In In re Wands, 8USPQ2d, 1400 (CAFC 1988) page 1404, the factors to be considered in determining whether a disclosure would require undue experimentation include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

First, the breadth of the claims is excessive with regard to claiming all polypeptides which are homologous to SEQ ID NO:116, or which have at least one conservative amino acid substitution, or for nucleic acid molecules encoding at least a portion of ion-x. Polynucleotides which comprise a portion of ion-x would have one or more nucleic acid substitutions, deletions, insertions and/or additions to said polynucleotide. Similarly, polypeptides which are homologous to, or have at least one conservative amino acid substitution to SEQ ID NO:116 would encode for a protein with one or more amino acid substitutions, deletions, insertions and/or additions to the protein encoded for by SEQ ID NO:116.

Applicants provide no guidance or working examples of polypeptides or polynucleotides which are of any length other than that of the full-length of SEQ ID NO:116 or its encoding nucleic acid, including molecules which are homologous to, substitution variants of SEQ ID NO:116, or portions of the

encoding nucleic acid molecule, nor do they provide a *function* of these nucleic acid molecules, or of the proteins which they encode. Furthermore, it is not predictable to one of ordinary skill in the art what the functions of these polynucleotides, or polypeptides are. Applicants have not taught which amino acids or nucleic acids are critical for function of the molecule. For example, there is no teachings of what amino acids are required to maintain the biological activity of any protein other than the full-length protein of SEQ ID NO:116. Finally, it is not predictable to the artisan how to make a functional polypeptide or polynucleotide which is less than the full-length of SEQ ID NO:116 since it is not predictable which residues or nucleic acids are critical for function of the molecule.

In summary, the breadth of the claims is excessive with regard to Applicants claiming all polypeptide and polynucleotides which are less than the full-length of SEQ ID NO:116 or nucleic acid molecules encoding ion-x, There is also a lack of guidance and working examples of these polypeptides and polynucleotides. Applicants do not provide a function of these polypeptides or polynucleotides which are other than the full-length molecules, nor do they provide any guidance as to which residues or nucleic acids are required to maintain function of these molecules. These factors, along with the lack of predictability to one of ordinary skill in the art as to how to make and use a functional polypeptide or polynucleotide other than the full-length molecules, leads the Examiner to hold that undue experimentation is necessary to practice the invention as claimed.

C. Claim 108 is rejected under 35 U.S.C. § 112, first and second paragraphs, as the claimed invention is not described in such full, clear, concise and exact terms as to enable any person skilled in the art to make and use the same, and/or for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claims include in scope allelic variants of the disclosed protein of SEQ ID NO:116. The Examiner could not find a definition of the term allelic variants in the specification. However, the art accepted meaning of allelic variant, is drawn exclusively to the state of a gene itself, and has no direct connotation regarding the protein encoded by the gene (it is noted that even genes or sequences which do not encode protein may exist as alleles). For example, Ayala and Kiger (Modern Genetics, Benjamin/Cumings 1980) define allele as "One of two or more alternative forms of a gene, each possessing a unique nucleotide sequence; different alleles of a given gene are usually recognized, however, by the phenotypes rather than by comparison of their nucleotide sequences." Thus, while allelic genes may result in a phenotypic change, the word does not have any particular connotation as to the encoded protein. Given this, the Examiner cannot determine how one would distinguish, merely by

examination of the protein, whether a protein were the result of expression of a different allele, or alternatively, were merely one of a number of ultimate species that might be obtained by the expression of one of the sequences particularly disclosed in this application. In addition, enablement is not commensurate in scope with claims to proteins encoded by allelic variants of the disclosed sequence. Allelic variants often encode proteins with quantitatively or qualitatively altered or absent biological activity. Therefore, the specification does not teach how to use such variants, nor is adequate guidance provided for the skilled artisan to predict, *a priori*, which variants would reasonably be expected to retain biological function.

6. Claim Rejections - 35 USC § 112, first paragraph – written description

A. Claims 105-109 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

These are genus claims. Polynucleotides which comprise "at least a portion" of ion-x would have one or more nucleic acid substitutions, deletions, insertions and/or additions to said polynucleotide. Similarly, polypeptides which are "homologous" to, or have "at least one conservative amino acid substitution" to SEQ ID NO:116 would encode for a protein with one or more amino acid substitutions, deletions, insertions and/or additions to the protein encoded for by SEQ ID NO:116.

The specification and claims do not indicate what distinguishing attributes are shared by the members of the genus. Thus the scope of the claims includes numerous structural variants, and the genus is highly variant because a significant number of structural differences between genus members is permitted. The specification and claims do not provide any guidance as to what changes should be made. Structural features that could distinguish compounds in the genus from others in the nucleic acid or protein class are missing from the disclosure. No common structural attributes identify the members of the genus. The general knowledge and level of skill in the art do not supplement the omitted description because specific, not general, guidance is what is needed. Since the disclosure fails to describe the common attributes or characteristics that identify members of the genus, and because the genus is highly variant, SEQ ID NO:116 alone are insufficient to describe the genus. One of skill in the art would reasonable conclude that the disclosure fails to provide a representative number of species to describe the genus. Thus, Applicant was not in possession of the claimed genus at the time the invention was made.

B. Claim 8 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The written description in this case only sets forth SEQ ID NO:116 and equivalent degenerative codon sequences thereof and therefore the written description is not commensurate in scope with the claims drawn to allelic variant sequences of a DNA molecule of SEQ ID NO:116.

Claim 8 is drawn to the genus including all DNA alleles encoding SEQ ID NO:116. The specification does not provide any particular definition for the term 'allele.' In this circumstance, the meaning of the term is the ordinary usage in the art. The ordinary meaning of the term 'allele' is one of two or more alternate forms of a gene occupying the same locus in a particular chromosome or linkage structure and differing from other alleles of the locus at one or more mutational sites. See, Rieger et al., *Glossary of Genetics* (1991), p. 16. The Rieger et al. reference discloses that there are at least seven different kinds of alleles in addition to the 'strictly neutral' type discussed above for claims 26-29. See Rieger, pp 16-17 (amorphs, hypomorphs, hypermorphs, antimorphs, neomorphs, isoalleles and unstable alleles). The alleles are distinguished by the effect their different structures have on phenotype. According to Rieger et al., alleles may differ functionally according to their distinct structures. For example, they may differ in the amount of biological activity the protein product may have, in the amount of protein produced, and/or the kind of activity the protein product will have.

Thus, the structure of naturally occurring allelic sequences are not defined. With the exception of SEQ ID NO:116, the skilled artisan cannot envision the detailed structure of the encompassed polynucleotides and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and a reference to a potential method of isolating it. The nucleic acid itself is required. See *Fiers v. Revel*, 25 USPQ 2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. V. Chugai Pharmaceutical Co. Lts.*, 18 USPQ2d 1016.

The specification discloses only one allele encoding the protein within the scope of the genus: that encoding SEQ ID NO:116. The specification proposes to discover other members of the genus by using a hybridization procedure. There is no description of the mutational sites that exist in nature, and there is no description of how the structure of the DNA encoding the claimed "allelic variants" relates to the structure of different alleles. In addition, according to the standard definition, the genus includes members that would be expected to have widely divergent functional properties. The general knowledge in the art concerning alleles does not provide any indication of how the structure of one allele is

representative of other unknown alleles having concordant or discordant functions. The common attributes of the genus are not described and the identifying attributes of individual alleles, other than that encoding SEQ ID NO:116 are not described. The nature of alleles is that they are variant structures where the structure of one does not provide guidance to the structure and function of others. According to these facts, one of skill in the art would conclude that the Applicant was not in possession of the claimed genus because a description of only one member of the genus is not representative of the variants of the genus and is insufficient to support the claim.

Vas-Cath Inc. V. Mahurkar, 19 USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention.* The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (*See Vas-Cath* at page 1116). Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 USC 112 is severable from its enablement provision (see page 115).

Furthermore, In *The Regents of the University of California v. Eli Lilly* (43 USPQ2d 1398-1412), the court held that a generic statement which defines a genus of nucleic acids by only their functional activity does not provide an adequate written description of the genus. The court indicated that while Applicants are not required to disclose every species encompassed by a genus, the description of a genus is achieved by the recitation of a representative number of DNA molecules, usually defined by a nucleotide sequence, falling within the scope of the claimed genus. At section B(1), the court states that "An adequate written description of a DNA...'requires a precise definition, such as by structure, formula, chemical name, or physical properties', not a mere wish or plan for obtaining the claimed chemical invention".

No disclosure, beyond the mere mention of allelic variants is made in the specification. This is insufficient to support the generic claims as provided by the Interim Written Description Guildlines published in the June 15, 1998 Federal Register at Volume 63, Number 114, pages 32639-32645.

Therefore only an isolated DNA molecule comprising a DNA sequence encoding SEQ ID NO:116 and equivalent degenerative codon sequences thereof, but not the full breadth of the claims meets the written description provision of 35 USC 112, first paragraph.

7. Claim Rejections - 35 USC § 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 105-109 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A. Claim 75, from which these claims ultimately depend, recite "ion-x." It appears that "ion-x" refers to various ion channels. The Examiner has reviewed Table I in the specification, but would appreciate an explanation of this term and how it relates to SEQ ID NO:116, the elected sequence. Claims 105-109 are rejected since they depend from claim 75.

B. Claims 105-109 are also rejected since the metes and bounds of "a portion of" in claim 75 are not known. This term could represent as few as one or two amino acids.

8. Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

A. Claims 106 and 107 are rejected under 35 U.S.C. 102(b) as being anticipated by Dubin et al. The claims recite a protein homologous to SEQ ID NO:116. Dubin et al. teach a protein which is 71.7% identical to SEQ ID NO:116 (Sequence Comparison A). This protein meets the limitation of "homologous" especially in the absence of any limitations or definition of the term "homologous."

B. Claims 106 and 107 are rejected under 35 U.S.C. 102(e) as being anticipated by Wood et al. (reference AC on the IDS submitted 1/30/03). The claims recite a protein homologous to SEQ ID NO:116. Wood et al. teach a protein which is 97.8% identical to SEQ ID NO:116 (Sequence Comparison B). This protein meets the limitation of "homologous" especially in the absence of any limitations or definition of the term "homologous."

9. Information Disclosure Statement

A. Reference AX on the IDS submitted 8/24/01 has been lined through since no publication year has been provided.

B. Reference DA on the IDS submitted 8/24/01 has been lined through since this information, as cited, is not appropriate for an IDS.

10. Conclusion

A. No claim is allowable.

Advisory information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert Landsman whose telephone number is (703) 306-3407. The examiner can normally be reached on Monday - Friday from 8:00 AM to 5:00 PM (Eastern time) and alternate Fridays from 8:00 AM to 5:00 PM (Eastern time).

If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, Gary Kunz, can be reached on (703) 308-4623.

Official papers filed by fax should be directed to (703) 308-4242. Fax draft or informal communications with the examiner should be directed to (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Robert Landsman, Ph.D.
Patent Examiner
Group 1600
August 01, 2003

ROBERT LANDSMAN
PATENT EXAMINER

Sequence Comparison A

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Q8WXA8
ID   Q8WXA8      PRELIMINARY;      PRT;   447 AA.
AC   Q8WXA8;
DT   01-MAR-2002 (TrEMBLrel. 20, Created)
DT   01-MAR-2002 (TrEMBLrel. 20, Last sequence update)
DT   01-JUN-2002 (TrEMBLrel. 21, Last annotation update)
DE   5-hydroxytryptamine receptor 3 subunit C.
GN   HTR3C.
OS   Homo sapiens (Human).
OC   Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC   Mammalia; Eutheria; Primates; Catarrhini; Hominidae; Homo.
OX   NCBI_TaxID=9606;
RN   [1]
RP   SEQUENCE FROM N.A.
RC   TISSUE=LUNG;
RA   Dubin A.E., Erlander M.G., Huvar A., Huvar R., Buehler L.K.;
RT   "DNA encoding a human subunit 5-HT3C of the 5HT3 serotonin receptor.";
RL   Submitted (DEC-2001) to the EMBL/GenBank/DDBJ databases.
DR   EMBL; AF459285; AAL66182.1; -.
DR   InterPro; IPR000188; GABAA_receptor.
DR   InterPro; IPR001175; Neur_channel.
DR   Pfam; PF02931; Neur_chan_LBD; 1.
DR   Pfam; PF02932; Neur_chan_memb; 1.
DR   PRINTS; PR00252; NRIONCHANNEL.
DR   PROSITE; PS00236; NEUROTR_ION_CHANNEL; UNKNOWN_1.
KW   Receptor.
SQ   SEQUENCE   447 AA;  50247 MW;  EA8146A2AAA2E1D7 CRC64;

  Query Match             71.7%;  Score 1781.5;  DB 4;  Length 447;
  Best Local Similarity   74.7%;  Pred. No. 8.8e-149;
  Matches  333;  Conservative   42;  Mismatches   62;  Indels    9;  Gaps    1;

Qy         26 ALLHLTHSMSTTGRGVTFTINCSGFGQHGADPTAVNSVFNRKPFRPVTNISVPTQVNISF 85
              ||| || |:   ||| |||||||| ||| ||    :||:|| ||| || |:||:|||||
Db         11 ALLCLTVSLLLQGRGDAFTINCSGFDQHGVDPAVFQAVFDRKAFRPFTNYSIPTRVNISF 70

Qy         86 AMSAILDVNEQLHLLSSFLWLEMVWDNPFISWNPEECEGITKMSMAAKNLWLPDIFIIEL 145
               :|||| |: || ||:||||:::|||||||:|||:|| || |::: |:||||||||:|
Db         71 TLSAILGVDAQLQLLTSFLWMDLVWDNPFINWNPKECVGINKLTVLAENLWLPDIFIVES 130

Qy        146 MDVDKTPKGLTAYVSNEGRIRYKKPMKVDSICNLDIFYFPFDQQNCTLTFSSFLYTVDSM 205
              ||||:|| |||||:|:||||:| |||:| ||| |||||||||||||| ||||||||||
Db        131 MDVDQTPSGLTAYISSEGRIKYDKPMRVTSICKLDIFYFPFDQQNCTFTFSSFLYTVDSM 190

Qy        206 LLDMEKEVWEITDASRNILQTHGEWELLGLSKATAKLSRGGNLYDQIVFYVAIRRRPSLY 265
              || |:|||||||| || ::|| |||||||::||| |:| | ||||||:||||||||||||
Db        191 LLGMDKEVWEITDTSRKVIQTQGEWELLGINKATPKMSMGNNLYDQIMFYVAIRRRPSLY 250

Qy        266 VINLLVPSGFLVAIDALSFYLPVKSGNRVPFKITLLLGYNVFLLMMSDLLPTSGTPLIGV 325
              :||||||| |||||||||||||| :| || ||||||||||||||||:|||| |||||| |
Db        251 IINLLVPSSFLVAIDALSFYLPAESENRAPFKITLLLGYNVFLLMMNDLLPASGTPLISV 310

Qy        326 YFALCLSLMVGSLLETIFITHLLHVATTQPPPLPRWLHSLLLHCNSPGRCCPTAPQKENK 385
              |||||||||| |||||:|||:||||||||||:|||||||||| |||||||||||  ||
Db        311 YFALCLSLMVVSLLETVFITYLLHVATTQPPPMPRWLHSLLLHCTSPGRCCPTAPQKGNK 370

Qy        386 GPGLTPTHLPGVKEPEVSAGQMPGPAEAELTGGSEWTRAQREHEAQKQHSVELWLQFSHA 445
              | ||| ||||| |||   ||:  || | |  ||| ||: |          :|||:|||||
Db        371 GLGLTLTHLPGPKEPGELAGKKLGPRETEPDGGSAWTKTQ---------LMELWVQFSHA 421

Qy        446 MDAMLFRLYLLFMASSIITVICLWNT 471
              || :|||||||||||||:||| ||||
Db        422 MDTLLFRLYLLFMASSILTVIVLWNT 447
```

Sequence Comparison B

```
ID   AAE10121 standard; Protein; 586 AA.
XX
AC   AAE10121;
XX
DT   29-NOV-2001  (first entry)
XX
DE   Human ion channel-31d6 (ion31d6) protein.
XX
KW   Human; ion channel-31d6; ion31d6;  antiinflammatory; immunosuppressive;
KW   analgesic; nootropic; neuroprotective; antidepressant; cardiant;
KW   cytostatic; antiviral; human immunodeficiency virus; HIV; anorectic;
KW   antiviral; thyroid disorder; thyrotoxicosis; myxoedema; renal failure;
KW   Crohn's disease; rheumatoid arthritis; autoimmune disorder; pain;
KW   stroke; psychotic disorder; neurological disorder; anxiety; dyskinesia;
KW   Huntington's disease; degenerative disorder; Parkinson's disease;
KW   schizophrenia; Alzheimer's disease; cardiovascular disease; cancer;
KW   metabolic disorder; anorexia; obesity; mental disorder.
XX
OS   Homo sapiens.
XX
FH   Key             Location/Qualifiers
FT   Misc-difference 469..470
FT                   /note= "Encoded by ACC TAG GCA"
FT   Misc-difference 503..504
FT                   /note= "Encoded by AGA TGA CTG"
FT   Misc-difference 517..518
FT                   /note= "Encoded by TGC TGA TCA"
FT   Misc-difference 541..542
FT                   /note= "Encoded by TTC TAG GTC"
FT   Misc-difference 548..549
FT                   /note= "Encoded by GCA TAG CAG"
FT   Misc-difference 561..562
FT                   /note= "Encoded by AAA TAA TTC"
XX
PN   WO200168849-A2.
XX
PD   20-SEP-2001.
XX
PF   09-MAR-2001; 2001WO-US07503.
XX
PR   10-MAR-2000; 2000US-0188400.
PR   10-MAR-2000; 2000US-0188517.
PR   10-MAR-2000; 2000US-0188518.
PR   10-MAR-2000; 2000US-0188519.
PR   05-JUL-2000; 2000US-0216815.
PR   06-JUL-2000; 2000US-0216481.
XX
PA   (PHAA ) PHARMACIA & UPJOHN CO.
XX
PI   Wood LS,  Vogeli G,  Karnovsky AM,  Ruble CL,  Linske-O'Connell LI;
PI   Wang J,  Liu D;
XX
DR   WPI; 2001-565795/63.
DR   N-PSDB; AAD17173.
XX
PT   New ion channel polynucleotides and polypeptides, useful for
PT   identification of ion channel modulators and treatment of mental
PT   disorders, infections, cancer and autoimmune diseases -
XX
PS   Claim 90; Page 101; 188pp; English.
XX
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CC The patent discloses novel human ion channel polypeptides and their
CC corresponding polynucleotides. The ion channel sequences and their
CC modulators are used for the treatment of viral infections (e.g. human
CC immunodeficiency virus (HIV)), thyroid disorders (e.g., thyrotoxicosis,
CC myxoedema), renal failure, inflammatory conditions (e.g., Crohn's
CC disease), rheumatoid arthritis, autoimmune disorders, pain, stroke,
CC psychotic and neurological disorders (e.g. anxiety, depression and
CC schizophrenia), dyskinesias (e.g. Huntington's disease), degenerative
CC disorders (e.g., Parkinson's disease, Alzheimer's disease), cardio-
CC vascular diseases, cancer, metabolic disorders (e.g. anorexia, obesity)
CC and mental disorders. The present sequence is ion channel-31d6 (ion31d6)
CC protein from human.
XX
SQ Sequence 586 AA;

Query Match 97.8%; Score 2429; DB 22; Length 586;
Best Local Similarity 99.8%; Pred. No. 8.1e-244;
Matches 459; Conservative 1; Mismatches 0; Indels 0; Gaps 0;

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Qy         12 RPALGPLSYREHRVALLHLTHSMSTTGRGVTFTINCSGFGQHGADPTAVNSVFNRKPFRP 71
              ||||||||||||||||||||||||||||||||||||||||||||||:||||||||||||
Db         10 RPALGPLSYREHRVALLHLTHSMSTTGRGVTFTINCSGFGQHGADPTALNSVFNRKPFRP 69

Qy         72 VTNISVPTQVNISFAMSAILDVNEQLHLLSSFLWLEMVWDNPFISWNPEECEGITKMSMA 131
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         70 VTNISVPTQVNISFAMSAILDVNEQLHLLSSFLWLEMVWDNPFISWNPEECEGITKMSMA 129

Qy        132 AKNLWLPDIFIIELMDVDKTPKGLTAYVSNEGRIRYKKPMKVDSICNLDIFYFPFDQQNC 191
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
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Qy        192 TLTFSSFLYTVDSMLLDMEKEVWEITDASRNILQTHGEWELLGLSKATAKLSRGGNLYDQ 251
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        190 TLTFSSFLYTVDSMLLDMEKEVWEITDASRNILQTHGEWELLGLSKATAKLSRGGNLYDQ 249

Qy        252 IVFYVAIRRRPSLYVINLLVPSGFLVAIDALSFYLPVKSGNRVPFKITLLLGYNVFLLMM 311
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        250 IVFYVAIRRRPSLYVINLLVPSGFLVAIDALSFYLPVKSGNRVPFKITLLLGYNVFLLMM 309

Qy        312 SDLLPTSGTPLIGVYFALCLSLMVGSLLETIFITHLLHVATTQPPPLPRWLHSLLLHCNS 371
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        310 SDLLPTSGTPLIGVYFALCLSLMVGSLLETIFITHLLHVATTQPPPLPRWLHSLLLHCNS 369

Qy        372 PGRCCPTAPQKENKGPGLTPTHLPGVKEPEVSAGQMPGPAEAELTGGSEWTRAQREHEAQ 431
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        370 PGRCCPTAPQKENKGPGLTPTHLPGVKEPEVSAGQMPGPAEAELTGGSEWTRAQREHEAQ 429

Qy        432 KQHSVELWLQFSHAMDAMLFRLYLLFMASSIITVICLWNT 471
              |||||||||||||||||||||||||||||||||||||||
Db        430 KQHSVELWLQFSHAMDAMLFRLYLLFMASSIITVICLWNT 469
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